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Substitute for form 1449B/PTO

## INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet

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of

9

### Complete If Known

Application Number	10/789,222
Filing Date	February 27, 2004
First Named Inventor	Qin Yu
Art Unit	Not Yet Assigned
Examiner Name	Not Yet Assigned

Attorney Docket Number UPN0003-100 (P3115)

### NON PATENT LITERATURE DOCUMENTS

Examiner Initials *	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
CFR	AA	FOLKMAN, "Tumor angiogenesis: therapeutic implications," New. Eng. J. Med. (1971) 285:1182-1186	
	AB	RISAU, "Mechanisms of angiogenesis," Nature (1997) 386:671-674.	
	AC	KIM, et al., "Inhibition of vascular endothelial growth factor-induced angiogenesis suppresses tumor growth in vivo," Nature (1993) 362:841-844.	
	AD	HANAHAN and FOLKMAN, "Patterns and emerging mechanisms for the angiogenic switch during tumorigenesis," Cell (1996) 86:353-364.	
	AE	HANAHAN, "Signalling vascular morphogenesis and maintenance," Science (1997) 277:48-50.	
	AF	HANAHAN and WEINBERG, "The hallmarks of cancer," Cell (2000) 100:57-70.	
	AG	FOLKMAN and D'AMORE, "Blood vessel formation: what is its molecular basis?", Cell (1986) 47:1153-1155.	
	AH	YANCOPOULOS, et al., "Vascular-specific growth factors and blood vessel formation," Nature (2000) 407:242-248.	
	AI	INGBER and FOLKMAN, "How does extracellular matrix control capillary morphogenesis?", Cell (1989) 58:803-805.	
	AJ	RAMSAUER and D'AMORE, "Getting tie(2)d up in angiogenesis," J. Clin. Investig. (2002) 110:1615-1617.	
↓	AK	BETSHOLTZ, et al., "Developmental roles of platelet-derived growth factors," BioEssays (2001) 23:494-507.	

Examiner Signature

Date Considered

6/11/06

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Sheet	2	of	9	Attorney Docket Number	UPN0003-100 (P3115)

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<i>JK</i>	AL	FONG, et al., "Role of the Flt-1 receptor tyrosine kinase in regulating the assembly of vascular endothelium," Nature (1995) 376:66-70.		T <sup>2</sup>
	AM	MAISONPIERRE, et al., "Angiopoietin-2, a natural antagonist for tie2 that disrupts in vivo angiogenesis," Science (1997) 277:55-60.		
	AN	SATO, et al., "tie-1 and tie-2 define another class of putative receptor tyrosine kinase genes expressed in early embryonic vascular system," Proc. Natl. Acad. Sci. USA (1993) 90:9355-9358.		
	AO	SCHNURCH and RISAU, "Expression of the tie-2, a member of a novel family of receptor tyrosine kinases, in the endothelial cell lineage," Development (1993) 119:957-968.		
	AP	DUMONT, et al., "Dominant-negative and targeted null mutations in the endothelial receptor tyrosine kinase, tek, reveal a critical role in vasculogenesis of the embryo," Genes Dev. (1994) 8:1897-1909.		
	AQ	COOGAN, et al., "Expression of tie2/tek in breast tumor vasculature provides a new marker for evaluation of tumor angiogenesis," Br. J. Cancer (1998) 77:51-58.		
	AR	SATO, et al., "Distinct roles of the receptor tyrosine kinases tie-1 and tie-2 in blood vessel formation," Nature (1995) 376:70-74.		
	AS	SURI, et al., "Requisite role of angiopoietin-1, a ligand for the TIE2 receptor during embryonic angiogenesis," Cell (1998) 87:1171-1180.		
	AT	GALE and YANCOPOULOS, "Growth factors acting via endothelial cell-specific receptor tyrosine kinases: VEGFs, angiopoietins, and ephrins in vascular development," Genes Dev. (1999) 13:1055-1066.		
	AU	SURI, et al., "Increased vascularization in mice overexpressing angiopoietin-1," Science (1998) 282:468-471.		
<i>✓</i>	AV	THURSTON, et al., "Leakage-resistant blood vessels in mice transenically overexpressing angiopoietin-1," Science (1999) 288:2511-2514.		

Examiner Signature	<i>Hope D'Souza</i>	Date Considered	9/11/06
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	AW	THURSTON, et al., "Angiopoietin-1 protects the adult vasculature against plasma leakage," <i>Nature Med.</i> (2000) 6:460-463.		T <sup>2</sup>
	AX	STRATMANN, et al., "Cell type-specific expression of angiopoietin-1 and angiopoietin-2 suggests a role in glioblastoma angiogenesis," <i>Am. J. Pathol.</i> (1998) 153:1459-1466.		
	AY	WITZENBICHLER, et al., "Chemotactic properties of angiopoietin-1 and -2, ligands for the endothelial-specific receptor tyrosine kinase tie2," <i>J. Biol. Chem.</i> (1998) 273:18514-18521.		
	AZ	CARLSON, et al., "Direct cell adhesion to the angiopoietins mediated by integrins," <i>J. Biol. Chem.</i> (2001) 276:26518-26525.		
	BA	PAPAPETROPOULOS, et al., "Angiopoietin-1 inhibits endothelial cell apoptosis via the Akt/survivin pathway," <i>J. Biol. Chem.</i> (2000) 275:9102-9105.		
	BB	KIM, et al., "Angiopoietin-1 regulates endothelial cell survival through the phosphatidylinositol 3'-kinase/Akt signal transduction pathway," <i>Circulation Res.</i> (2000) 86:24-29.		
	BC	HAYES, et al., "Angiopoietin-1 and its receptor Tie-2 participate in the regulation of capillary-like tubulin formation and survival of endothelial cells," <i>Microvasc. Res.</i> (1999) 58:224-237.		
	BD	OH, et al., "Hypoxia and vascular endothelial growth factor selectively upregulate angiopoietin-2 in bovine microvascular endothelial cells," <i>J. Biol. Chem.</i> (1999) 274:15732-15739.		
	BE	MANDRIOTA and PEPPER, "Regulation of angiopoietin-2 mRNA levels in bovine microvascular endothelial cells by cytokines and hypoxia," <i>Circulation Res.</i> (1998) 83:852-859.		
	BF	KIM, et al., "Tumor necrosis factor-alpha upregulates angiopoietin-2 in human umbilical vein endothelial cells," <i>Biochem. Biophys. Res. Comm.</i> (2000) 269:361-365.		
	BG	KIM, et al., "Angiopoietin-1 induces endothelial cell sprouting through the activation of focal adhesion kinase and plasmin secretion," <i>Circulation Res.</i> (2000) 86:952-959.		

Examiner Signature	<i>AprerRobinson</i>	Date Considered	6/11/06
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CH	BH	VALENZUELA, et al., "Angiopoietins 3 and 4: diverging gene counterparts in mice and humans," Proc. Natl. Acad. Sci. USA (1999) 96:1904-1909.		T <sup>2</sup>
	BI	SIEMEISTER, et al., "Two independent mechanisms essential for tumor angiogenesis: inhibition of human melanoma xenograft growth by interfering with either the vascular endothelial growth factor receptor pathway or the tie-2 pathway," Cancer Res. (1999) 59:3185-3193.		
	BJ	MILLAUER, et al., "Glioblastoma growth inhibited in vivo by a dominant-negative Flk-1 mutant," Nature (1994) 367:576-579.		
	BK	GOLDMAN, et al., "Paracrine expression of a native soluble vascular endothelial growth factor receptor inhibits tumor growth, metastasis, and mortality rate," Proc. Natl. Acad. Sci. USA (1998) 95:8795-8800.		
	BL	AHMAD, et al., "The effects of angiopoietin-1 and -2 on tumor growth and angiogenesis in human colon cancer," Cancer Res. (2001) 61:1255-1259.		
	BM	ETOH, et al., "Angiopoietin-2 is related to tumor angiogenesis in gastric carcinoma: possible in vivo regulation via induction of proteases," Cancer Res. (2001) 61:2145-2153.		
	BN	HAWIGHORST, et al., "Activation of the tie2 receptor by angiopoietin-1 enhances tumor vessel maturation and impairs squamous cell carcinoma growth," Am. J. Pathol. (2002) 160:1381-1392.		
	BO	KOGA, et al., "Expression of angiopoietin-2 in human glioma cells and its role for angiogenesis," Cancer Res. (2001) 61:6248-6254.		
	BP	PAPETTI and HERMAN, "Mechanisms of normal and tumor-derived angiogenesis," Am. J. Physiol. Cell Physiol. (2002) 282:C947-C970.		
	BQ	TEICHERT-KULISZEWSKA, et al., "Biological action of angiopoietin-2 in a fibrin matrix model of angiogenesis is associated with activation of Tie2," Cardiovasc. Res. (2001) 49:659-670.		
✓				

Examiner Signature	<i>Chen Zhenyu</i>	Date Considered	01/11/06
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YIA	BS	YU and STAMENKOVIC, "Localization of matrix metalloproteinase 9 to the cell surface provides a mechanism for CD44-mediated tumor invasion," Genes Dev. (1999) 13:35-48.		
	BT	HUNGERFORD and LITTLE, "Developmental biology of the vascular smooth muscle cell: building a multilayered vessel wall," J. Vasc. Res. (1999) 36:2-27.		
	BU	GALE, et al., "Angiopoietin-2 is required for postnatal angiogenesis and lymphatic patterning, and only the latter role is rescued by angiopoietin-1," Devel. Cell (2002) 3:411-423.		
	BV	SHYU, et al., "Direct intramuscular injection of plasmid DNA encoding angiopoietin-1 but not angiopoietin-2 augments revascularization in the rabbit ischemic hindlimb," Circulation (1998) 98:2081-2087.		
	BW	KIM, et al., "Angiopoietin-2 at high concentration can enhance endothelial cell survival through the phosphatidylinositol 3'-kinase/Akt signal transduction pathway," Oncogene (2000) 19:4549-4552.		
	BX	LANDER and SELLECK, "The elusive functions of proteoglycans: in vivo veritas," J. Cell Biol. (2000) 148:227-232.		
	BY	IOZZO, "Matrix metalloproteins: from molecular design to cellular function," Ann. Rev. Biochem. (1998) 67:609-652.		
	BZ	IOZZO and SAN ANTONIO, "Heparan sulfate proteoglycans: heavy hitters in the angiogenesis arena," J. Clin. Investig. (2001) 108:349-355.		
	CA	FIEDLER, et al., "Angiopoietin-1 and angiopoietin-2 share the same binding domains in the tie-2 receptor involving the first Ig-like loop and the epidermal growth factor-like repeats," J. Biol. Chem. (2003) 278:1721-1727.		
	CB	YU, et al., "Induction of apoptosis of metastatic mammary carcinoma cells in vivo by disruption of tumor cell surface CD44 function," J. Exp. Med. (1997) 186:1985-1998.		
✓	CC	KONTOS, et al., "Tyrosine 1011 of tie2 is the major site of association of p85 and is required for activation of phosphatidylinositol 3'-kinase and Akt," Mol. Cell. Biol. (1998) 18:4131-4140.		

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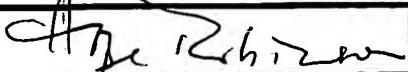
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CH	CD	FIDLER and ELLIS, "The Implications of angiogenesis for the biology and therapy of cancer metastasis," <i>Cell</i> (1994) 78:185-188.		
	CE	FIDLER, "Angiogenetic heterogeneity: regulation of neoplastic angiogenesis by the organ microenvironment," <i>J. Natl. Cancer Inst.</i> (2001) 93:1040-1041.		
	CF	ALI, et al., "Estrogen receptor-alpha in the inhibition of cancer growth and angiogenesis," <i>Cancer Res.</i> (2000) 60:7094-7098.		
	CG	NOKIHARA, et al., "Natural killer cell-dependent suppression of systemic spread of human lung adenocarcinoma cells by monocyte chemoattractant protein-1 gene transfection in severe combined immunodeficient mice," <i>Cancer Res.</i> (2000) 60:7002-7007.		
	CH	LINDAHL, et al., "Pericyte loss and microaneurysm formation in PDGF-B-deficient mice," <i>Science</i> (1997) 277:242-245.		
	CI	GENGROVITCH, et al., "Glypican-1 is a VEGF165 binding proteoglycan that acts as an extracellular chaperone for VEGF165," <i>J. Biol. Chem.</i> (1999) 274:10818-10822.		
	CJ	LI, et al., "Increased responsiveness of hypoxic endothelial cells to FGF2 is mediated by HIF-1alpha-dependent regulation of enzymes involved in synthesis of heparan sulfate FGF2-binding sites," <i>J. Cell Sci.</i> (2002) 115:1951-1959.		
	CK	NEUFELD, et al., "Vascular endothelial growth factor (VEGF) and its receptors," <i>FASEB J.</i> (1999) 13:9-22.		
	CL	PARK, et al., "The vascular endothelial growth factor (VEGF) isoforms: differential deposition into the subepithelial extracellular matrix and bioactivity of extracellular matrix-bound VEGF," <i>Mol. Biol. Cell</i> (1993) 4:1317-1328.		
	CM	PEPPER, et al., "Transforming growth factor-beta: vasculogenesis, angiogenesis, and vessel wall integrity," <i>Cytokine Growth Factor Rev.</i> (1997) 8:21-43.		
✓	CN	XU and YU, "E-cadherin negatively regulates CD44-hyaluronan interaction and CD44-mediated tumor invasion and branching morphogenesis," <i>J. Biol. Chem.</i> (2003) 278:8681-8688.		

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<i>JK</i>	CO	POLTORAK, et al., "VEGF145, a secreted vascular endothelial growth factor isoform that binds to extracellular matrix," <i>J. Biol. Chem.</i> (1997) 272:7151-7158.		
	CP	ROBINSON and STRINGER, "The splice variants of vascular endothelial growth factor (VEGF) and their receptors," <i>J. Cell Sci.</i> (2001) 114:853-865.		
	CQ	RUHRBERG, "Endogenous inhibitors of angiogenesis," <i>J. Cell Sci.</i> (2001) 114:3215-3216.		
	CR	SAARISTO, et al., "Mechanisms of angiogenesis and their use in the inhibition of tumor growth and metastasis," <i>Oncogene</i> (2000) 19:6122-6129.		
	CS	MAESHIMA, et al., "Tumstatin, an endothelial cell-specific inhibitor of protein synthesis," <i>Science</i> (2002) 285:140-143.		
	CT	O'REILLY, et al., "Angiostatin: a novel angiogenesis inhibitor that mediates the suppression of metastases by a Lewis lung carcinoma," <i>Cell</i> (1994) 79:315-328.		
	CU	O'REILLY, et al., "Antiangiogenic activity of the cleaved conformation of the serpin antithrombin," <i>Science</i> (1999) 285:1926-1928.		
	CV	YI and RUOSLAHTI, "A fibronectin fragment inhibits tumor growth, angiogenesis, and metastasis," <i>Proc. Natl. Acad. Sci. USA</i> (2001) 98:620-624.		
	CW	VU, et al., "MMP-9/gelatinase-B is a key regulator of growth plate angiogenesis and apoptosis of hypertrophic chondrocytes," <i>Cell</i> (1998) 93:411-422.		
	CX	VAJKOCZY, et al., "Microtumor growth initiates angiogenic sprouting with angiogenic sprouting with simultaneous expression of VEGF, VEGF receptor-2, and angiopoietin-2," <i>J. Clin. Investig.</i> (2002) 109:777-785.		
<i>V</i>	CY	BLOEMENDAL, et al., "New strategies in anti-vascular cancer therapy," <i>Eur. J. Clin. Investig.</i> (1999) 29:802-809.		

Examiner Signature	<i>Stephanie Johnson</i>	Date Considered	6/11/06
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<sup>1</sup>Applicant's unique citation designation number (optional). <sup>2</sup>Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO in process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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Substitute for form 1448B/PTO				Complete if Known	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>				<i>Application Number</i>	10/789,222
(Use as many sheets as necessary)				<i>Filing Date</i>	February 27, 2004
				<i>First Named Inventor</i>	Qin Yu
				<i>Art Unit</i>	Not Yet Assigned
				<i>Examiner Name</i>	Not Yet Assigned
Sheet	8	of	9	<i>Attorney Docket Number</i>	UPN0003-100 (P3115)

NON PATENT LITERATURE DOCUMENTS				
Examiner Initials *	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.		
<i>AFR</i>	CZ	HARFOUCHE, et al., "Mechanisms which mediate the antiapoptotic effects of angiopoietin-1 on endothelial cells," <i>Microvasc. Res.</i> (2002) 64:135-147.		T <sup>2</sup>
	DA	HIRAOKA, et al., "Matrix metalloproteinases regulate neovascularization by acting as pericellular fibrinolysins," <i>Cell</i> (1998) 95:365-377.		
	DB	BERGERS, et al., "Matrix metalloproteinase-9 triggers the angiogenic switch during carcinogenesis," <i>Nature Cell Biol.</i> (2000) 2:737-744.		
	DC	FANG, et al., "Matrix metalloproteinase-2 is required for the switch to the angiogenic phenotype in a tumor model," <i>Proc. Natl. Acad. Sci. USA</i> (2000) 97:3884-3889.		
	DD	PFEIFER, et al., "Suppression of angiogenesis by lentiviral delivery of PEX, a noncatalytic fragment of matrix metalloproteinase 2," <i>Proc. Natl. Acad. Sci. USA</i> (2000) 97:12227-12232.		
	DE	STERNLICHT and WERB, "How matrix metalloproteinases regulate cell behavior," <i>Ann. Rev. Cell Dev. Biol.</i> (2001) 17:463-518.		
	DF	SILLETTI, et al., "Disruption of matrix metalloproteinase 2 binding to integrin alphavbeta3 by an organic molecule inhibits angiogenesis and tumor growth in vivo," <i>Proc. Natl. Acad. Sci. USA</i> (2001) 98:119-124.		
	DG	SIPES, et al., "Cooperation between thrombospondin-1 type 1 repeat peptides and alphavbeta3 integrin ligands to promote melanoma cell spreading and focal adhesion kinase phosphorylation," <i>J. Biol. Chem.</i> (1999) 274:22755-22762.		
	DH	VISCONTI, et al., "Orchestration of angiogenesis and arteriovenous contribution by angiopoietins and vascular endothelial growth factor (VEGF)," <i>Proc. Natl. Acad. Sci. USA</i> (2002) 99:8219-8224.		
	DI	UEMURA, et al., "Recombinant angiopoietin-1 restores higher-order architecture of growing blood vessels in mice in the absence of mural cells," <i>J. Clin. Invest.</i> (2002) 110:1619-1628.		
<i>(✓)</i>	DJ	YU and STMENKOVIC, "Cell surface-localized matrix metalloproteinase-9 proteolytically activates TGF-beta and promotes tumor invasion and angiogenesis," <i>Genes Dev.</i> (2000) 14:163-176.		

Examiner Signature	<i>Chase Eshenroder</i>	Date Considered	6/16/06
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Substitute for form 1449B/PTO				Complete if Known	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>				<i>Application Number</i>	10/789,222
(Use as many sheets as necessary)				<i>Filing Date</i>	February 27, 2004
				<i>First Named Inventor</i>	Qin Yu
				<i>Art Unit</i>	Not Yet Assigned
				<i>Examiner Name</i>	Not Yet Assigned
Sheet	9	of	9	Attorney Docket Number	UPN0003-100 (P3115)

NON PATENT LITERATURE DOCUMENTS				
Examiner Initials *	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.		T <sup>2</sup>
	DK	McFALL and RAPRAEGER, "Characterization of the high affinity cell-binding domain in the cell surface proteoglycan syndecan-4," J. Biol. Chem. (1998) 273:28270-28276.		
	DL	OLSON, et al., "High affinity binding of latent matrix metalloproteinase-9 to the alpha2(IV) chain of collagen IV," J. Biol. Chem. (1998) 273:10672-10681.		
	DM	BROOKS, et al., "Localization of matrix metalloproteinase MMP-2 to the surface of invasive cells by interaction with integrin alphavbeta3," Cell (1996) 85:683-693.		
	DN	MOYON, et al., "Selective expression of angiopoietin 1and 2 in mesenchymal cells surrounding veins and arteries of the avian embryo," Mechs. Devel. (2001) 106:133-136.		
	DO	WONG, et al., "Tie2 expression and phosphorylation in angiogenic and quiescent adult tissues," Circ. Res. (1997) 81:567-574.		
	DP	SHIM, et al., "Inhibition of angiopoietin-1 expression in tumor cells by an antisense RNA approach inhibited xenograft tumor growth in immunodeficient mice," Int. J. Cancer (2001) 94:6-15.		
	DQ	SHIM, et al., "Angiopoietin 1 promotes tumor angiogenesis and tumor vessel plasticity of human cervical cancer in mice," Exp. Cell Res. (2002) 279:299-309.		
	DR	JOUSSEN, et al., "Suppression of diabetic retinopathy with angiopoietin-1," Am. J. Pathol. (2002) 160:1683-1693.		
	DS	HATTORI, et al., "Vascular endothelial growth factor and angiopoietin-1 stimulate postnatal hematopoiesis by recruitment of vasculogenic and hematopoietic stem cells," J. Exp. Med. (2001) 193:1005-1014.		
	DT	DAVIS, et al., "Angiopoietins have distinct modular domains essential for receptor binding, dimerization and superclustering," Nature Struct. Biol. (2002) 10:38-44.		

Examiner Signature	<i>Christopher R. Johnson</i>	Date Considered	6/11/06
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## **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**

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Sheet 1 of 1

Complete if Known	
Application Number	10/789,222
Filing Date	February 27, 2004
First Named Inventor	Qin Yu
Art Unit	To Be Determined
Examiner Name	To Be Determined
Attorney Docket Number	UPN0003-100 (P3115)

#### **NON-PATENT LITERATURE DOCUMENTS**

**Examiner  
Signature**

George Robinson

Date Considered

6/11/04

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